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THE EFFECTS OF STIMULATING CAROTID CHEMORECEPTORS ON RENAL HAEMODYNAMICS AND FUNCTION IN DOGS

BY F. KARIM*, S. M. POUCHER† AND R. A. SUMMERILL
From the Department of Physiology, University of Leeds, Leeds LS2 9JT

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SUMMARY

1. Dogs were anaesthetized with chloralose and artificially ventilated. The carotid chemoreceptors were stimulated by changing the perfusion of vascularly isolated carotid sinus regions from arterial to venous blood. The mean carotid sinus pressure and the mean arterial blood pressure were held constant at 124 ± 3 and 122 ± 3 mmHg, respectively. Both vagosympathetic trunks were sectioned in the neck and propranolol (17 μg kg^{-1} min^{-1} I.V.) and gallamine triethiodide (0·2–2·0 mg kg^{-1} 30 min^{-1} I.V.) were infused. Renal blood flow was measured by an electromagnetic flow probe, glomerular filtration rate by creatinine clearance, sodium excretion by flame photometry and solute excretion by osmometry.

2. In sixteen tests in thirteen dogs perfusion of the carotid sinus regions with venous blood resulted in significant decreases in renal blood flow from 271 ± 24 to 198 ± 21 ml min^{-1} 100 g^{-1} renal mass; glomerular filtration rate from $41{\cdot}0 \pm 4{\cdot}8$ to $22{\cdot}1 \pm 3{\cdot}1$ ml min^{-1} 100 g^{-1}; filtration fraction from $0{\cdot}25 \pm 0{\cdot}02$ to $0{\cdot}19 \pm 0{\cdot}02$; urine flow from $0{\cdot}48 \pm 1{\cdot}0$ to $0{\cdot}21 \pm 0{\cdot}03$ ml min^{-1} 100 g^{-1}; sodium excretion from $18{\cdot}1 \pm 4{\cdot}1$ to $12{\cdot}9 \pm 4{\cdot}2$ μmol min^{-1} 100 g^{-1}; and osmolar excretion 327 ± 42 to 171 ± 26 μosmol min^{-1} 100 g^{-1}. The right atrial pressure did not change significantly from $4{\cdot}6 \pm 1{\cdot}2$ cmH_2O.

3. In seven dogs, tying renal sympathetic nerves abolished all the responses except that of sodium excretion which was now reversed; sodium excretion increased from 68 ± 19 to 116 ± 38 μmol min^{-1} 100 g^{-1} without significant change in right atrial pressure from $7{\cdot}4 \pm 1{\cdot}9$ cmH_2O. Crushing the carotid bodies, however, abolished all the responses.

4. The results show that carotid chemoreceptor stimulation can cause significant reflex effects on renal haemodynamics and function which are mediated via renal sympathetic nerves. They also show that the chemoreceptor stimulation can cause natriuresis in the absence of haemodynamic changes, in the denervated kidney, presumably via a humoral factor.

INTRODUCTION

It has been reported that patients with acute respiratory failure show an increase in water retention (Kilburn & Dowell, 1971) and an increase in plasma level of antidiuretic hormone (Szatalowicz, Goldberg & Anderson, 1982) during severe hy-

* To whom correspondence should be sent at the above address.

† Present address: Biosciences II, ICI Pharmaceuticals Ltd, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG.

poxia. However, most of the studies in which the whole animal has been subjected to hypoxia, hypercapnia or acidosis have produced no consistent effects (Norman, MacIntyre, Shearer, Craigen & Smith, 1970; Bruns, 1978; Anderson, Pluss, Berns, Jackson, Arnold, Schrier & McDonald, 1978; Waker, 1982; Rose, Kimmel, Godine, Kaiser & Carey, 1983; Rose, Anderson & Carey, 1984). The mechanisms of the renal responses to these generalized changes in blood gases and acid–base status are not known for certain.

Localized stimulation of the carotid chemoreceptors causes an increase in renal nerve activity (Linden, Mary & Weatherill, 1981) and a decrease in renal blood flow (Little & Oberg, 1975; Kappagoda, Karim & Mackay, 1983). It has also been reported that carotid chemoreceptor stimulation increases sodium excretion (Fischer, Honig, Meyer & Rauhut, 1969; Flemming, Honig, Potzschke, Rauhut, Roloff, Roth & Schulze, 1971; Honig, Flemming, Rauhut, Roloff, Boge, Matthies & Walther, 1975; Honig, Schmidt & Freyse, 1979; Schmidt, Ledderhos & Honig, 1985). However, since arterial blood pressure was not controlled in most of these studies the natriuretic response could have been secondary to changes in renal haemodynamics.

The aim of the present experiments was: (1) to determine, in anaesthetized dogs, the effects on renal haemodynamics and function of stimulation of carotid chemoreceptors by perfusing the vascularly isolated carotid sinus regions with venous blood under conditions of constant aortic pressure and (2) to examine the afferent and efferent mechanisms of this reflex action.

METHODS

Thirteen greyhounds (23·6–32·4 kg) of both sexes were anaesthetized with thiopentone sodium (Intraval Sodium; May & Baker; 500 mg I.V.) followed by α-chloralose (Rentokil; 0·1 g kg^{-1} I.V.). These were administered through a catheter that had been passed under local anaesthesia (2% xylocaine, Astra Pharmaceuticals) via the right lateral saphenous vein so that the tip lay in the inferior vena cava. Surgical anaesthesia was maintained by a constant infusion of chloralose (0·3 mg kg^{-1} min^{-1}). The chloralose was dissolved in a solution of isotonic saline (0·9%, w/v) to achieve a final concentration of 10 mg ml^{-1}. The trachea was exposed through a mid-line incision and cannulated. Positive-pressure ventilation, with 40% oxygen in air, was started using a Starling Ideal Pump at a rate of 18 strokes min^{-1} and a stroke volume of approximately 15 ml kg^{-1}.

The carotid sinus regions were vascularly isolated and perfused with blood either from one of the common carotid arteries (baroreceptor stimulation) or from one of the femoral veins (chemoreceptor stimulation) at a constant flow as described previously (Karim, Mackay & Kappagoda, 1982*b*; Kappagoda *et al.* 1983; Karim, Poucher & Summerill, 1984) (Fig. 1). The blood perfusing the regions was drained into an external jugular vein through a polyethylene cannula placed in both external carotid arteries. Samples of blood were collected from the cannulae to measure P_{O_2}, P_{CO_2} and pH of the blood perfusing the chemoreceptors. Before connecting the perfusion circuits to the animals, heparin was given (185 units kg^{-1} I.V.; Evans Medical) followed by a continuous infusion into the carotid circuit at approximately 1 unit kg^{-1} min^{-1}.

In all animals the left renal artery and ureter were exposed retroperitoneally and prepared for measurement of blood flow and urine collection as described previously (Karim *et al.* 1984). In three of the dogs the right kidney was similarly prepared. In two of them the left kidney was supplied by two arteries with separate origins from the aorta, so the total blood flow was measured by using two flow probes (4 and 3·5 mm I.D., model SP 7515, Gould Statham, CA, U.S.A.); zero flow was determined by occlusion of the renal artery distal to the probes. The flowmeters (Gould Statham, model SP2202) were calibrated by placing the probe around the common carotid artery which was perfused with the animal's own blood using a roller pump; the calibration factor was then obtained by timed collection of blood at several rates. In seven dogs a loose tie was placed around the sympathetic nerves supplying the left kidney.

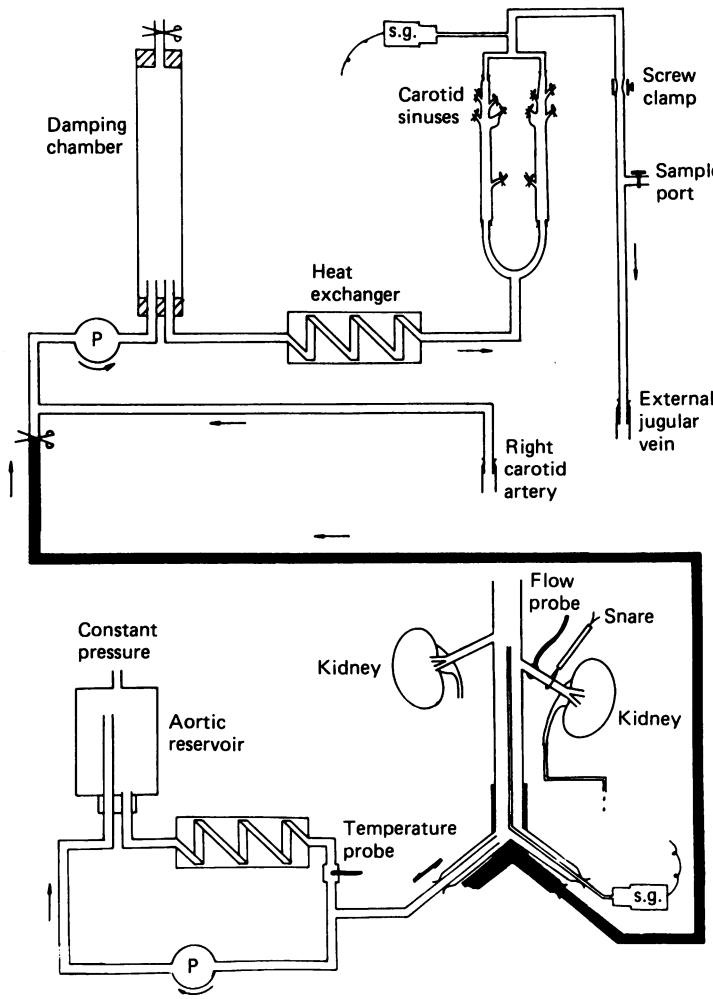


Fig. 1. Diagram of experimental preparation. Vascularly isolated carotid sinus regions were perfused at a constant flow with either arterial blood from the right common carotid artery, or venous blood from the left femoral vein. The blood was pumped through a damping chamber and heat exchanger using a roller pump (P). Carotid sinus pressure as recorded by a strain gauge (s.g.) was set at the desired level by regulating the outflow resistance by a screw-clamp and blood from the carotid sinuses returned to an external jugular vein. Renal blood flow was measured using a flow probe. Aortic pressure was held constant by connecting the descending aorta to a reservoir maintained at a constant pressure by means of a Starling resistance and compressed air. Blood in the system was kept warm by circulating it through a heat exchanger by means of a pump. Arrows indicate direction of flow of blood.

Aortic pressure (renal perfusion pressure) was measured through a cannula which was passed through the cardiac end of the left femoral artery so that its tip lay in the abdominal aorta close to the origin of the left renal artery. Right atrial pressure was measured through a cannula inserted via an external jugular vein. Pressures were recorded with Statham strain gauges (Model P23 ID) connected to appropriate cannulae. The mean pressure in the abdominal aorta was controlled by connecting it to a reservoir maintained at a constant pressure by means of a Starling resistance and compressed air (Karim *et al.* 1984).

At least 50 min before the first clearance period a continuous infusion of creatinine solution (10 mM, in a mixture of 50% dextran solution, Dextraven 150, Fisons Pharmaceuticals Ltd; and 50% isotonic saline solution, 0·9%, w/v, Travenol) was started by means of an infusion pump (Harvard, model 975 A) via the catheter in the inferior vena cava. The infusion of this solution was continued throughout the experiment at 2 ml min^{-1} for determination of glomerular filtration rate. Creatinine in plasma and urine was determined by autoanalyser (Technicon) using the Jaffe reaction. Urinary sodium was determined by flame photometry (Corning-Eel 400) and osmolarity by freezing point depression (Roebling micro-osmometer). Urinary pH and blood gases and pH were measured periodically (Corning 161 pH/blood gas analyser). The vagosympathetic trunks were sectioned in the neck to eliminate influence of cardiopulmonary receptors, propranolol (17 μg kg^{-1} min^{-1}) was infused to prevent heart rate change (Karim, Kidd, Malpus & Penna, 1972) and gallamine triethiodide (Flaxedil, May & Baker, 0·2–2·0 mg kg^{-1} 30 min^{-1}) was infused to prevent respiratory movements.

Experimental protocol

About an hour after the perfusion circuit had been connected to the dog, the following procedures were carried out. Arterial blood gases and pH were adjusted to the normal range, and the carotid sinus and aortic pressures were set at desired levels (122±3 and 124±3 mmHg, respectively). When all measured variables were steady, urine collection was started for two consecutive 10 min periods; at the third minute of each period an arterial blood sample (about 2 ml) was taken for plasma creatinine determination. The carotid chemoreceptors were then stimulated by changing their perfusion from arterial blood to venous blood from the left femoral vein (see Fig. 1). The carotid sinus pressure and the renal perfusion pressure (aortic pressure) were held constant. No further collections were taken until at least 3 ml of urine (estimated dead space of the kidney and ureteral cannula) was passed. A further two consecutive urine collections were then made as before (10 or 20 min when urine volume was low). This procedure was repeated after changing the carotid perfusion back to arterial blood and an equilibration period of about 20 min. This procedure was repeated in seven dogs after ligation of the renal sympathetic nerves and in three dogs after crushing the carotid bodies with a fine arterial clamp.

Statistical methods

The statistical significance of the values was determined by using a t test for paired observations except that of sodium excretion where Wilcoxon's signed rank test was applied (see Table 1). Differences between groups were deemed non-significant at $P > 0·05$. All values quoted are the mean±S.E. of the mean.

RESULTS

Blood gas status, pH and other variables

The mean values of arterial pH, P_{O_2}, P_{CO_2} and temperature were 7·42±0·01, 142±8 mmHg, 40·3±0·6 mmHg and 37·5+0·02 °C, respectively. Plasma sodium concentration and plasma osmolality were 144·6±2·6 mM and 308±2·0 mosM, respectively. The values of pH, P_{O_2}, and P_{CO_2} of the venous blood perfusing the carotid sinus regions were 7·32±0·01, 27·4±0·8 mmHg and 45·3±1·2 mmHg, respectively.

Effect of vagotomy on renal blood flow

The carotid sinus regions were perfused with arterial blood at a constant pressure of 128±7 mmHg. Cutting both vagus nerves between ligatures in the neck resulted in an immediate increase in systemic arterial pressure and a decrease in renal blood flow. When aortic pressure was corrected to the pre-vagotomy control level (127±7 mmHg before and 131±5 mmHg after vagotomy) the renal blood flow was decreased by 14±3% ($P < 0·01$) from a control value of 298±28 ml min^{-1} 100 g^{-1}. Figure 2 shows a typical record from one of the experiments.

Cardiovascular responses to perfusing carotid sinus regions with venous blood

Seven tests were performed in three dogs prior to vagotomy and infusion of propranolol. Venous perfusion of the carotid chemoreceptors resulted in the usual bradycardia and a rise in systemic arterial blood pressure. The heart rate decreased significantly from 143 ± 15 to 104 ± 5 beats min^{-1} ($P < 0{\cdot}02$) whilst mean arterial

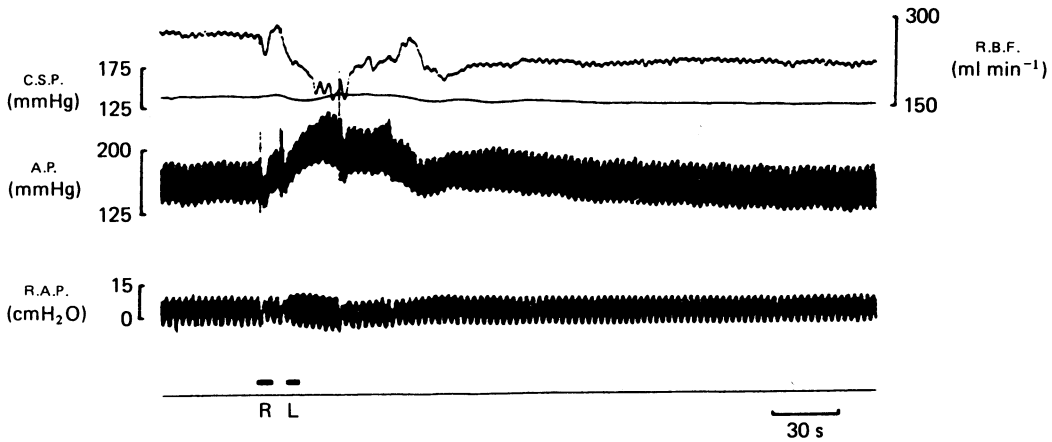


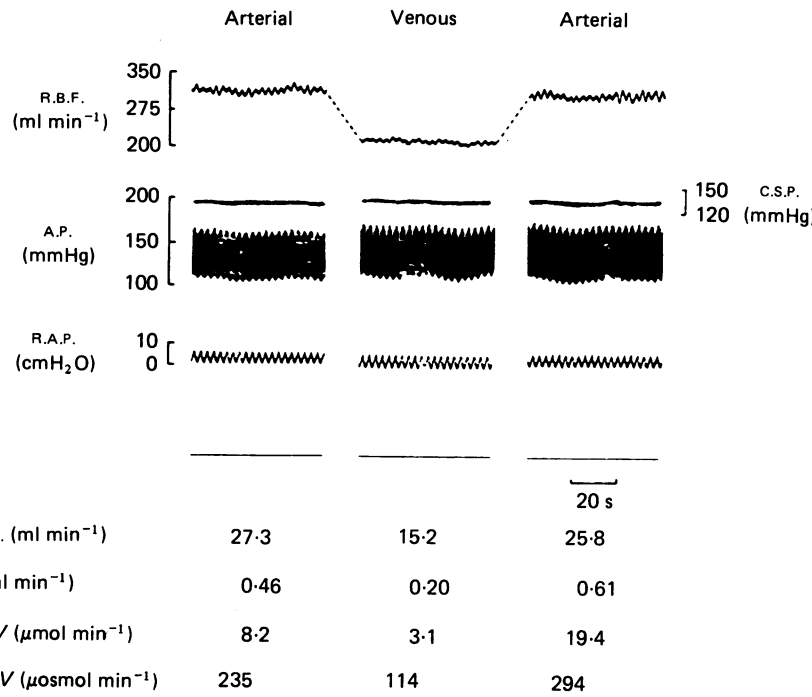
Fig. 2. Records showing the renal blood flow (R.B.F.) and systemic arterial pressure (A.P.) responses to cutting the right (R) and left (L) vagus nerves. C.S.P., carotid sinus pressure; R.A.P., right atrial pressure. Note that vagotomy resulted in a dramatic fall in renal blood flow, even though systemic arterial pressure showed a concomitant rise to a very high value.

pressure increased significantly from 129 ± 4 to 154 ± 5 mmHg ($P < 0{\cdot}001$). When the perfusion was changed back to arterial blood the heart rate increased to 144 ± 15 beats min^{-1} ($P < 0{\cdot}02$) and mean arterial blood pressure decreased to 126 ± 4 mmHg ($P < 0{\cdot}001$). The heart rate response was abolished after vagotomy and propranolol infusion, whilst the effect on the blood pressure persisted. The aortic pressure was controlled during subsequent chemoreceptor stimulation. The mean right atrial pressure during these tests did not change significantly either before denervation of the kidney from $4{\cdot}6 \pm 1{\cdot}2$ cmH_2O or after from $7{\cdot}4 \pm 1{\cdot}9$ cmH_2O (Fig. 4).

Renal responses to perfusion of the carotid chemoreceptor with venous blood

During these tests carotid sinus pressure was held constant. Since the responses were similar in tests in which carotid sinus perfusion sequence was arterial–venous–arterial to those in which the sequence was arterial–venous, the two values with arterial perfusion have been averaged and compared to that with venous perfusion. Figure 3 shows a typical example of the experimental records and values obtained from one of the tests and Fig. 4 shows summarized results from sixteen intact kidneys in thirteen dogs. In all cases, perfusing the carotid sinus regions with venous blood resulted in significant decreases in renal blood flow from 271 ± 24 to 198 ± 21 ml min^{-1} 100 g^{-1} ($P < 0{\cdot}001$); glomerular filtration rate from $41 \pm 4{\cdot}8$ to $22{\cdot}1 \pm 3{\cdot}1$ ml min^{-1} 100 g^{-1} ($P < 0{\cdot}001$); filtration fraction from $0{\cdot}25 \pm 0{\cdot}02$ to 0·19

$\pm 0{\cdot}2$ ($P < 0{\cdot}01$); urine flow from $0{\cdot}48 \pm 0{\cdot}10$ to $0{\cdot}21 \pm 0{\cdot}03$ ml min^{-1} 100 g^{-1} ($P < 0{\cdot}02$); sodium excretion from $18{\cdot}1 \pm 4{\cdot}1$ to $12{\cdot}9 \pm 4{\cdot}2$ μmol min^{-1} 100 g^{-1} ($P < 0{\cdot}05$) and osmolar excretion 327 ± 42 to 171 ± 26 μosmol min^{-1} 100 g^{-1} ($P < 0{\cdot}01$). However, the changes in urinary sodium concentration (from $43{\cdot}8 \pm 8{\cdot}8$ to $50{\cdot}5 \pm 10{\cdot}5$ mM) and fractional sodium excretion (from $0{\cdot}35 \pm 0{\cdot}10$ to $0{\cdot}46 \pm 0{\cdot}14$) were not significant.



G.F.R. (ml min^{-1})	27·3	15·2	25·8
V (ml min^{-1})	0·46	0·20	0·61
$U_{Na}V$ (μmol min^{-1})	8·2	3·1	19·4
$U_{osm}V$ (μosmol min^{-1})	235	114	294

Fig. 3. Records and values showing renal responses to carotid chemoreceptor stimulation at constant carotid sinus (C.S.P.) and constant arterial pressure (A.P). R.B.F., renal blood flow; G.F.R., glomerular filtration rate; V, urine flow; $U_{Na}V$, sodium excretion; $U_{osm}V$, osmolar excretion; R.A.P., right atrial pressure. Perfusion of carotid sinus regions with venous blood caused renal blood flow to decrease from 318 to 214 ml min^{-1}, which increased to 300 ml min^{-1} upon returning the perfusion to arterial. The intervals between traces were at least 20 min each.

Effect of renal nerve ligation upon renal responses

In seven dogs the effects of renal nerve ligation upon the renal responses were investigated. In all animals, ligation of the renal nerves abolished all of the renal responses except sodium excretion (Fig. 4 and Table 1). There was a consistent increase in urinary sodium concentration and sodium excretion in response to stimulation of carotid chemoreceptors in all of the denervated kidneys. The increase in sodium concentration was statistically significant ($P < 0{\cdot}01$). However, although the changes in sodium excretion (mean increase 48 μmol min^{-1} 100 g^{-1}) were not significant as judged by paired t test, they were significant ($P < 0{\cdot}01$) when Wilcoxon's signed rank test was applied to the data (see Fig. 4 and Table 1). This sodium

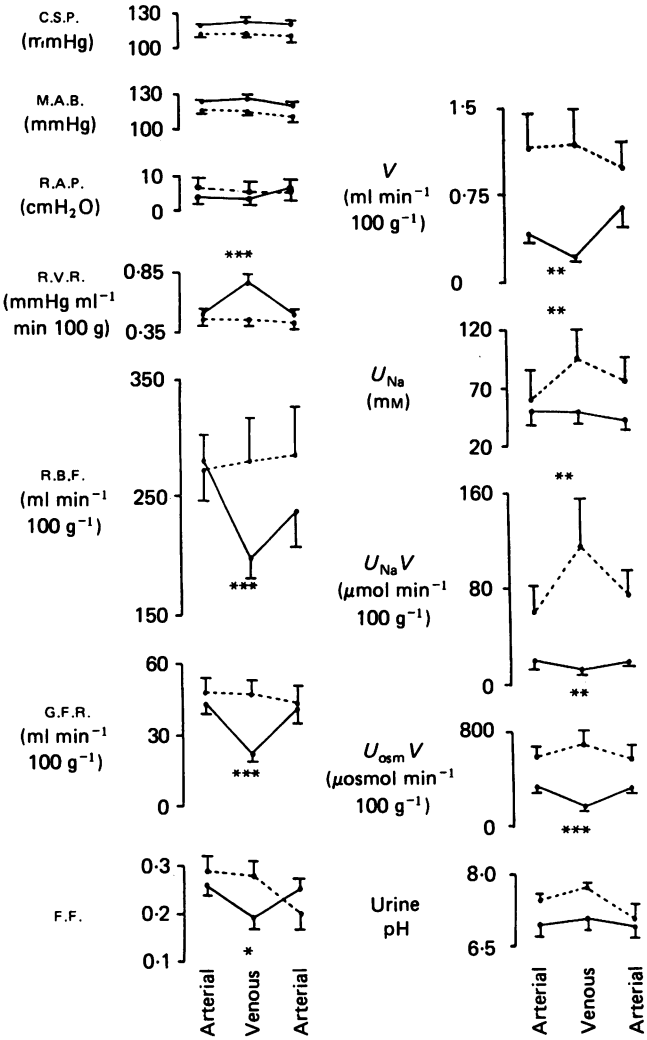


Fig. 4. The response to carotid chemoreceptor stimulation in intact ($n = 16$, continuous lines), and denervated ($n = 7$, broken lines) kidneys. Each point shows the mean value with standard error of the mean. All values were statistically compared with the initial level in that series. Where no symbol is present, $P > 0{\cdot}05$; otherwise, $*P < 0{\cdot}02$; $**P < 0{\cdot}01$; $***P < 0{\cdot}001$. M.A.P., mean arterial pressure; M.R.A.P., mean right atrial pressure; R.V.R., renal vascular resistance; F.F., filtration fraction; U_{Na}, urinary sodium concentration; other abbreviations are the same as in Figs 2 and 3.

excretion response in the denervated kidney was a complete reversal of that seen before renal nerve ligation.

Renal responses after destruction of carotid body chemoreceptors

Although the bradycardia before vagotomy indicates that carotid chemoreceptors were being stimulated, the receptors responsible for the renal effects were investigated further. After observing the usual renal responses, the carotid sinus region was

TABLE 1. Renal responses to carotid chemoreceptor stimulation after renal nerve ligation

	M.A.P		R.B.F.		G.F.R.		F.F		$\dot{V}$		U_{Na}		$U_{Na}\dot{V}$		$U_{osm}\dot{V}$	
Dog number	Arterial	Venous	Arterial	Venous	Arterial	Venous	Arterial	Venous	Arterial	Venous	Arterial	Venous	Arterial	Venous	Arterial	Venous
1	124	116	377	400	59·8	64·3	0·270	0·267	0·83	0·71	48·6	66·0	40·5	46·9	710	710
2	96	100	301	311	49·9	41·9	0·230	0·187	0·42	0·52	179·2	200·0	76·1	104·5	437	539
3	105	103	256	249	25·8	24·8	0·143	0·153	1·85	1·49	23·9	37·3	38·7	54·9	350	382
4	100	110	134	141	27·0	30·7	0·210	0·365	0·29	0·58	5·7	22·3	1·5	14·9	213	393
5	115	119	227	195	48·7	52·4	0·328	0·400	1·49	2·63	59·7	113·0	94·1	297·6	696	1148
6	120	124	268	272	35·6	43·5	0·237	0·288	1·69	1·49	97·4	141·0	162·6	210·6	653	754
13	130	134	387	394	71·0	69·8	0·292	0·278	0·94	0·92	67·1	91·8	61·2	83·9	1019	1006
Mean	113	115	279	280	45·4	46·8	0·244	0·277	1·07	1·19	68·8	95·9	67·8	116·2	583	705
S.E. of mean	5	4	33	36	6·4	6·3	0·023	0·033	0·23	0·28	21·5	23·4	19·4	38·4	102	111
P	n.s.		n.s.		n.s.		n.s.		n.s.		$< 0·01$*		$< 0·01$**		n.s.	

The values of renal variables have been normalized and expressed as per 100 g renal mass, hence units of R.B.F., G.F.R. and $\dot{V}$ are ml min^{-1} $100\ g^{-1}$; $U_{Na}\dot{V}$ is μmol min^{-1} $100\ g^{-1}$; $U_{osm}\dot{V}$ is μosmol min^{-1} $100\ g^{-1}$. M.A.P., mean arterial pressure; other abbreviations and units as in Figs 3 and 4. Arterial values were obtained when the carotid bodies were perfused with arterial blood and venous values obtained when they were perfused with venous blood. Note that ligation of the renal nerves abolished the renal responses to carotid chemoreceptor stimulation; however, the effect of sodium concentration and excretion were reversed. * Paired t test. ** Wilcoxon's signed rank test.

perfused with venous blood after either crushing the carotid bodies or tying ligatures around the origins of both occipital arteries. The reflex systemic pressure response was reduced but not completely abolished during venous perfusion of the carotid sinus region indicating that not all of the receptors were damaged. However, after this procedure, perfusion of the carotid sinus regions with venous blood had no effect on the kidney.

DISCUSSION

The present experiments have shown that perfusion of carotid sinus regions with venous blood in dogs anaesthetized with chloralose, at constant carotid and aortic pressure, results in significant decreases in renal blood flow, glomerular filtration rate, filtration fraction, urine flow, sodium and solute excretion but not fractional sodium excretion (Fig. 4). These effects were mediated by a reflex with its receptors in the carotid bodies and its efferent pathway in the renal sympathetic nerves. Our experiments have also shown that the effect on sodium excretion can be reversed by ligation of the renal nerves (Fig. 4 and Table 1).

Since the carotid sinus regions were vascularly isolated, the effects were not the result of venous perfusion of the brain. The effectiveness of the isolation was checked during calibration of the flow probe at the end of the experiment (see Methods). It was observed that the inflow of blood into the carotid sinus regions was equal to the outflow collected into a measuring cylinder. The responses were also unlikely to be the result of any inhibition by the venous blood of the carotid baroreceptor activity, because the heart rate response was a bradycardia and not a baroreceptor-induced tachycardia. The details of this method of stimulation of the carotid bodies have been described elsewhere (Hainsworth, Karim & Sofola, 1979; Karim, Hainsworth, Sofola & Wood, 1980). That the reflex originated in the carotid bodies was indicated by the fact that it was abolished by crushing them.

The changes were unlikely to be influenced by any changes in the activities of the receptors in the cardiopulmonary areas and chest wall during stimulation of the carotid chemoreceptors (Daly & Scott, 1962; Karim *et al.* 1972; Karim, Kaufman & Kappagoda, 1982*a*), because (1) the animals were artificially ventilated, (2) the skeletal muscle was paralysed by gallamine administration and (3) the vagosympathetic trunks were sectioned in the neck.

The changes in renal blood flow in responses to stimulation of the carotid chemoreceptors observed in the intact kidneys in this study were consistent with that reported by Mancia (1975), Little & Oberg (1975), Kappagoda *et al.* (1983), Marshall (1981), Rose *et al.* (1983, 1984) and Schmidt *et al.* (1985) on anaesthetized cats and dogs. Also, the changes in sodium excretion in the denervated kidneys were not different from that reported by Fischer *et al.* (1969), Flemming *et al.* (1971), Honig *et al.* (1975, 1979) and Schmidt *et al.* (1985) in spontaneously breathing cats with intact kidneys. They observed an increase in sodium excretion during chemoreceptor stimulation and this effect was larger in the denervated kidney. Although species differences cannot be entirely ruled out, the differences in responses could also be the result of either the renal nerves already having been damaged or the chemoreceptor stimulation not being adequate to bring about a large enough change in renal sympathetic nerve activity for haemodynamic (Karim *et al.* 1984) and tubular effects

(DiBona, 1978) in their experiments. However, we have also seen an increase in sodium excretion during chemoreceptor stimulation, but only after ligation of the renal nerves. This extremely interesting finding suggests that the reflex effect on sodium excretion was mediated by a humoral factor.

It is known that localized stimulus to the carotid body chemoreceptors in anaesthetized dogs causes a significant release of antidiuretic hormone (Share & Levy, 1966). This antidiuretic hormone or any other humoral factor was unlikely to have any significant effects, because the responses were completely abolished by denervation of the kidney. Any significant contribution from changes in angiotensin level was also unlikely because the release of renin was minimized by administration of propranolol (Johns, Lewis & Singer, 1976; Osborn, Holdaas, Thames & DiBona, 1983; Blair, Chen & Izzo, 1985).

The exact mechanism by which renal nerves mediate the antidiuretic and antinatriuretic responses in our experiments are uncertain. The fall in renal blood flow and glomerular filtration rate produced by renal vasoconstriction could largely be responsible for the changes in urine flow (O'Connor & Summerill, 1979). However, a direct action of the renal nerves on the kidney tubules cannot be entirely ruled out (DiBona, 1978).

The increases in urinary sodium concentration and sodium excretion during carotid chemoreceptor stimulation after renal nerve ligation occurred in all seven experiments (Table 1), even though the baseline level of sodium excretion increased to about 300% of that in the intact kidney (Fig. 4). One possible explanation for the absence of this response in the intact kidney could be that carotid chemoreceptor stimulation led to the release of a 'natriuretic' factor which, when the renal nerves were intact, was unable to overcome the stimulatory effects of the nerves on the vasculature and the tubular system for sodium reabsorption (DiBona, 1978). But when freed from these constraints, i.e. after denervation of the kidney, the natriuretic factor was capable of increasing the sodium and osmolar excretion without much change in urine flow. It would be interesting to know whether a moderate degree of chemoreceptor stimulation that does not produce a big change in renal haemodynamics and function, can show a chemoreceptor-induced natriuresis and diuresis in the intact kidney.

The origin and nature of the natriuretic factor involved in these experiments are uncertain. The atrial natriuretic factor is unlikely to have contributed to the responses for several reasons. (a) Since propranolol prevented both chronotropic and inotropic changes, and aortic pressure was maintained constant, the right atrial pressure did not change significantly during chemoreceptor stimulation (see Fig. 4). (b) In a similar preparation, in which propranolol and atropine were used and aortic pressure was controlled, the left atrial pressure did not change significantly during chemoreceptor stimulation (Kappagoda *et al.* 1983). (c) The usual effect of atrial natriuretic peptide of increasing glomerular filtration rate, even in the face of concomitant decrease in mean arterial pressure, was absent in the renal responses (Maack, Marion, Camargo, Kleinert, Laragh, Vaughan & Atlas, 1984; Cogan, 1986; Sosa, Volpe, Marion, Atlas, Laragh, Vaughan & Maack, 1986). The involvement of a hypothalamic natriuretic factor or any other humoral factor remains to be determined.

So far as we know, the present investigation is the first in which the renal response to carotid chemoreceptor stimulation has been demonstrated with full control of other variables in dogs and where the reduction of renal function has been completely abolished by denervation of the kidney. Our work has also demonstrated that the natriuretic responses to carotid chemoreceptor stimulation may be mediated by a humoral factor. However, the role of the arterial chemoreceptors in the daily regulation of sodium excretion (Honig, Schmidt, Arndt, Karnz & Rogoll, 1985) remains to be confirmed.

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